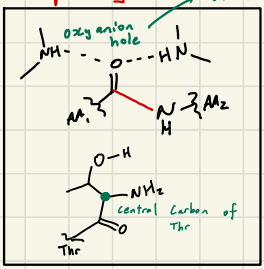
Alternate nucleophile / ↑electrophilicity

Threonine Proteases



① Thr as 1st nucleophile

② 1st tetrahedral intermediate

③ H_2O as 2nd nucleophile

④ 2nd tetrahedral intermediate

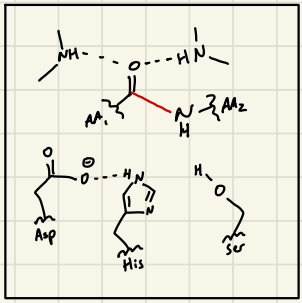
P.T.

Serine/Cysteine Protease

Asp+His+Ser ↑ His + Cys

OH SH ← more polarizable, doesn't need Asp

(example is Ser Protease)



① Asp/enzyme environment raises His pKa
↳ His deprotonates Ser (or Cys)

② Ser (or Cys) as 1st nuc.

③ 1st tetrahedral int.

④ H_2O as 2nd nuc.

P.T.

④ 2nd tetrahedral int.